

## General

### Guideline Title

Summary of evidence-based guideline: periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. Report of the Guideline Development Subcommittee of the American Academy of Neurology.

### Bibliographic Source(s)

Armstrong MJ, Gronseth G, Anderson DC, Biller J, Cucchiara B, Dafer R, Goldstein LB, Schneck M, Messing SR. Summary of evidence-based guideline: periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2013 May 28;80(22):2065-9. [7 references]  
[PubMed](#)

### Guideline Status

This is the current release of the guideline.

The American Academy of Neurology (AAN) reaffirmed the currency of the guideline in January 2016.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

Definitions for the strength of evidence (Class I-IV) and strength of recommendations (Level A-U) are located at the end of the Major Recommendations Field.

1. It is axiomatic that clinicians managing antithrombotic medications periprocedurally weigh bleeding risks from drug continuation against thromboembolic (TE) risks from discontinuation at the individual patient level, although high-quality evidence on which to base this decision is often unavailable. In addition, even when evidence is insufficient to exclude a difference in bleeding or shows a small increase in clinically important bleeding with antithrombotic agents, physicians may reasonably judge that the risks and morbidity of TE events exceed those associated with bleeding.
2. Neurologists should counsel both patients taking aspirin for secondary stroke prevention and their physicians that aspirin discontinuation is probably associated with increased stroke and transient ischemic attack (TIA) risk (Level B). Estimated stroke risks vary across studies and according to duration of aspirin discontinuation.
3. Neurologists should counsel patients taking anticoagulation (AC) for stroke prevention that the TE risks associated with different AC periprocedural management strategies (continuing oral AC or stopping it with or without bridging heparin) are unknown (Level U) but that the risk of TE complications with warfarin discontinuation is probably higher if AC is stopped for  $\geq 7$  days (Level B).
4. Patients taking aspirin should be counseled that aspirin continuation is highly unlikely to increase clinically important bleeding complications

- with dental procedures (Level A). Given minimal clinically important bleeding risks, it is reasonable that stroke patients undergoing dental procedures should routinely continue aspirin (Level A).
5. Patients taking aspirin should be counseled that aspirin continuation probably does not increase clinically important bleeding complications with invasive ocular anesthesia, cataract surgery, dermatologic procedures, transrectal ultrasound–guided prostate biopsy, spinal/epidural procedures, and carpal tunnel surgery (Level B). Given minimal clinically important bleeding risks, it is reasonable that stroke patients undergoing these procedures should probably continue aspirin (Level B).
  6. Aspirin continuation might not increase clinically important bleeding in vitreoretinal surgery, electromyogram (EMG), transbronchial lung biopsy, colonoscopic polypectomy, upper endoscopy with biopsy, sphincterotomy, and abdominal ultrasound–guided biopsies. Given the weaker data supporting minimal clinically important bleeding risks, it is reasonable that some stroke patients undergoing these procedures should possibly continue aspirin (Level C).
  7. Although bleeding events were rare, studies of transurethral resection of the prostate lack the statistical precision to exclude clinically important bleeding risks with aspirin continuation (Level U).
  8. Patients taking aspirin should be counseled that aspirin probably increases bleeding risks during orthopedic hip procedures (Level B).
  9. Neurologists should counsel patients that there is insufficient evidence to make recommendations regarding appropriate periprocedural clopidogrel, ticlopidine, or aspirin/dipyridamole management in most situations (Level U). Aspirin recommendations cannot be extrapolated with certainty to other antiplatelet (AP) agents.
  10. Patients taking warfarin should be counseled that warfarin continuation is highly unlikely to be associated with increased clinically important bleeding complications with dental procedures (Level A). Given minimal bleeding risks, stroke patients undergoing dental procedures should routinely continue warfarin (Level A).
  11. Patients taking warfarin should be counseled that warfarin continuation is probably associated with only a small (1.2%) increased risk difference for bleeding during dermatologic procedures on the basis of a meta-analysis of heterogeneous and conflicting studies (Level B). Thus, patients undergoing dermatologic procedures should probably continue warfarin (Level B).
  12. Patients taking warfarin should be counseled that warfarin continuation is probably not associated with an increased risk of clinically important bleeding with ocular anesthesia (Level B). However, AC practices during ophthalmologic procedures may be driven by the postanesthesia procedure. Although bleeding events were rare, ophthalmologic studies (other than those regarding ocular anesthesia) lack the statistical precision to exclude clinically important bleeding risks with warfarin continuation. Thus, there is insufficient evidence to make practice recommendations regarding warfarin discontinuation in ophthalmologic procedures (Level U).
  13. Warfarin might be associated with no increased clinically important bleeding with EMG, prostate procedures, inguinal herniorrhaphy, and endothermal ablation of the great saphenous vein. Thus, patients undergoing these procedures should possibly continue warfarin (Level C).
  14. Patients taking warfarin should be counseled that warfarin continuation might increase bleeding with colonoscopic polypectomy (Level C). Thus, patients undergoing this procedure should possibly temporarily discontinue warfarin (Level C).
  15. Neurologists should counsel patients that there is insufficient evidence to make recommendations regarding appropriate periprocedural management of nonwarfarin oral AC (Level U). Warfarin recommendations cannot be extrapolated with certainty to other AC agents.
  16. There is insufficient evidence to determine differences in TE in chronically anticoagulated patients managed with heparin bridging therapy relative to oral AC discontinuation or continuation. Patients taking warfarin should be counseled that bridging therapy is probably associated with increased bleeding risks in procedures in general relative to AC cessation (Level B). Bridging probably does not reduce clinically important bleeding relative to continued AC with warfarin in dentistry, but bleeding risk differences between patients managed with continued warfarin vs bridging therapy in other procedures are unknown. Given that the benefits of bridging therapy are not established and that bridging is probably associated with increased bleeding risks, there is insufficient evidence to support or refute bridging therapy use in general (Level U).

#### Definitions:

##### Strength of Evidence

Class I: A cohort study of a broad spectrum of persons at risk for developing the outcome (e.g., target disease, work status). The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class II: A case control study of a broad spectrum of persons with the condition compared to a broad spectrum of controls or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class III: A case control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or

measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV: Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

#### Strength of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)\*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome > 5 and the lower limit of the confidence interval is > 2).

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

Ischemic cerebrovascular disease

### Guideline Category

Counseling

Management

Risk Assessment

Treatment

### Clinical Specialty

Neurology

Surgery

### Intended Users

Physicians

### Guideline Objective(s)

- To assess evidence regarding periprocedural management of antithrombotic drugs in patients with ischemic cerebrovascular disease

- To provide evidence-based recommendations regarding periprocedural management of patients with a history of ischemic cerebrovascular disease receiving anticoagulation (AC) or antiplatelet (AP) agents
- To answer the following clinical questions:
  - What is the thromboembolic (TE) risk of temporarily discontinuing an antithrombotic medication?
  - What are the perioperative bleeding risks of continuing antithrombotic agents?
  - If oral AC is stopped, should bridging therapy be used?
  - If an antithrombotic agent is stopped, what should be the timing of discontinuation?

## Target Population

Patients with ischemic cerebrovascular disease

## Interventions and Practices Considered

1. Weigh bleeding risks from drug continuation against thromboembolic (TE) risks from discontinuation at the individual patient level
2. Counsel patients and their physicians on specific risks of drug discontinuation or continuation
3. Drug continuation or discontinuation (in appropriate circumstances)
  - Aspirin
  - Warfarin
  - Clopidogrel
  - Ticlopidine
  - Dipyridamole
  - Heparin bridging therapy

## Major Outcomes Considered

Incidence and severity of:

- Vascular events
- Reoperation
- Transfusion
- Moderate or severe bleeding
- Clinically important specialty-specific outcomes (e.g., vision loss due to hemorrhage with ophthalmologic procedures or paralysis due to hemorrhage during spinal epidural procedures)

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

#### 2013 Guideline

Literature searches of MEDLINE and EMBASE through August 2011 were performed in all languages using relevant MeSH terms, text word synonyms, and key words (for search strategy, see appendices e-3 and e-4 in the data supplement [see the "Availability of Companion Documents" field]). The searches identified 5,904 citations yielding 133 relevant articles which at least two authors rated by using American Academy of Neurology (AAN) prognostic classification criteria (see appendix e-5 in the data supplement [see the "Availability of Companion Documents" field]). Studies were downgraded one level for indirectness of evidence (e.g., comparing patients continuing antithrombotic agents with nonusers rather than with patients discontinuing medication). Bleeding and thromboembolic (TE) risks were analyzed by intervention type.

Recommendations were linked to evidence strength (see appendix e-6 in the data supplement [see the "Availability of Companion Documents" field]).

Articles were included if they studied patients taking oral antithrombotic agents for primary or secondary cardiovascular disease or stroke prevention (including articles relating to atrial fibrillation), studied at least 20 subjects, included a comparison group, assessed risks of continuing or discontinuing an agent, and clearly described interventions and outcome measures. Both cardiac and stroke patients were included because risks overlap and many studies do not distinguish between the two groups. Case reports, review papers, and articles studying coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, pacemaker/defibrillator placement, and cerebrovascular procedures such as carotid endarterectomy were excluded because of confounding issues (e.g., procedure-related stroke) and because this guideline focuses on antithrombotic questions posed to treating neurologists. Non-English-language articles were included for which translations could be obtained.

#### 2016 Reaffirmation

MEDLINE was searched from August 2011 to January 2016 using the search terms cerebrovascular accident OR cerebrovascular disorders AND Platelet Aggregation Inhibitors, antiplatelet, Aspirin, clopidogrel, Plavix, Ticlopidine, Anti-Inflammatory Agents, Non-Steroidal AND postoperative complications. Inclusion/exclusion criteria for the search included RCTs, humans only, relevant to clinical questions; criteria used to screen search results were the same as described in the 2013 published guideline.

## Number of Source Documents

133

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

### Classification of Evidence for Prognostic Studies

Class I: A cohort study of a broad spectrum of persons at risk for developing the outcome (e.g., target disease, work status). The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class II: A case control study of a broad spectrum of persons with the condition compared to a broad spectrum of controls or a cohort study of a broad spectrum of persons at risk for the outcome (e.g., target disease, work status) where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who is masked to the presence of the risk factor. Study results allow calculation of measures of prognostic accuracy.

Class III: A case control study or a cohort study where either the persons with the condition or the controls are of a narrow spectrum where the data was collected retrospectively. The outcome is defined by an acceptable reference standard for case definition. The outcome is objective or measured by an observer who did not determine the presence of the risk factor. Study results allow calculation of measures of a prognostic accuracy.

Class IV: Studies not meeting Class I, II, or III criteria, including consensus, expert opinion, or a case report.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

The panel considered clinically relevant outcomes (e.g., vascular events, reoperation, transfusion) rather than surrogate markers (e.g., hemoglobin level). Bleeding was classified according to GUSTO criteria (see figure e-1 in the data supplement [see the "Availability of Companion Documents" field]). Moderate or severe bleeding was considered clinically important. Consideration was also given to clinically important specialty-specific outcomes, such as vision loss due to hemorrhage with ophthalmologic procedures or paralysis due to hemorrhage during spinal epidural procedures. Where possible, the risk difference (RD) – the arithmetic difference between the proportion of patients in one group experiencing the event relative to the proportion of patients in the other group – was calculated. The authors used 95% confidence intervals (CIs) of the RDs (calculated using Wilson's method) as the measure of statistical precision.

Studies with the highest evidence levels for each intervention are discussed in the text of the original guideline document. All studies are presented in the evidence table (see table e-1 in the data supplement [see the "Availability of Companion Documents" field]), including Class III studies that did not inform recommendations.

## Methods Used to Formulate the Recommendations

### Expert Consensus

## Description of Methods Used to Formulate the Recommendations

### 2013 Guideline

The American Academy of Neurology (AAN) Guideline Development Subcommittee (see appendices e-1 and e-2 in the data supplement [see the "Availability of Companion Documents" field]) convened an expert panel to develop the guideline. Recommendations were made that were linked to the evidence (see appendix e-6 in the data supplement [see the "Availability of Companion Documents" field]).

### 2016 Reaffirmation

A Guideline Development, Dissemination, and Implementation (GDDI) member who had expertise in stroke and vascular neurology conducted a targeted literature search for high quality studies using the same criteria as presented in the original guideline. The GDDI reviewer and the subcommittee reviewed the new evidence and determined that the following three criteria were met: 1. There is no new evidence that would alter conclusions or recommendations in the guideline since the last literature search, 2. Guideline methodology is sound and current methodology is not substantially different, and 3. No significant practice variation relevant to the guideline currently exists.

## Rating Scheme for the Strength of the Recommendations

### Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)\*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

\*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome > 5 and the lower limit of the confidence interval is > 2).

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

Drafts of the original guideline document were reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields.

The guideline was approved by the AAN Guideline Development Subcommittee on July 14, 2012; by the AAN Practice Committee on August 3, 2012; and by the AAN Board of Directors on January 17, 2013.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease

### Potential Harms

- Stopping antithrombotics increases the risk of thromboembolic (TE) events. The exact magnitude of this risk increase is unknown. To minimize this risk, it seems reasonable to minimize the duration of antithrombotic discontinuation.
- When considering the risks and benefits of antithrombotic discontinuation, it is important to consider both the frequency of undesirable outcomes and their long-term consequences. TE events occur infrequently, but the associated morbidity and mortality rates are high. In contrast, most reported bleeding outcomes are relatively mild. Decisions regarding periprocedural antithrombotic therapy depend on weighing these competing risks in the context of individual patient characteristics.

## Qualifying Statements

### Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. Formal practice recommendations are not intended to replace clinical judgment.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Living with Illness

### IOM Domain

Effectiveness

## Identifying Information and Availability

### Bibliographic Source(s)

Armstrong MJ, Gronseth G, Anderson DC, Biller J, Cucchiara B, Dafer R, Goldstein LB, Schneck M, Messing SR. Summary of evidence-based guideline: periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2013 May 28;80(22):2065-9. [7 references]  
[PubMed](#)

### Adaptation

Not applicable: the guideline was not adapted from another source.

### Date Released

2013 May 28 (reaffirmed 2016 Jan 23)

### Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society



## Source(s) of Funding

American Academy of Neurology (AAN)

## Guideline Committee

Guideline Development Subcommittee of the American Academy of Neurology (AAN)

## Composition of Group That Authored the Guideline

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## Financial Disclosures/Conflicts of Interest

### Conflict of Interest

The American Academy of Neurology (AAN) is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, Neurology® peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at the [AAN Web site](#)

### Disclosures

M.J. Armstrong, G. Gronseth, D.C. Anderson, J. Biller, B. Cucchiara, R. Dafer, and L.B. Goldstein report no disclosures.

M. Schneck has participated in the past 2 years as a local principal investigator for multicenter trials sponsored by the National Institutes of Health (NIH), Lundbeck Pharmaceuticals, Brigham & Women's/Schering Plough (Thrombolysis in Myocardial Infarction consortium), Gore Inc., and NMT Medical. He is currently working on an investigator-initiated project to be supported by Baxter, Inc. He has served on speakers' bureaus for Boehringer-Ingelheim and Bristol-Myers Sanofi (none in past 2 years); has received an honorarium from the American Academy of Neurology Continuum project, from UpToDate.com, and from various continuing medical education lectures; and has participated in expert testimony for medical malpractice cases. He has no significant stock or other financial conflicts of interest.

S.R. Messé has received royalties for articles on antithrombotics and stroke published on UpToDate.com. He has also received research support from the NIH for a study of the pharmacogenomics of warfarin and a study to evaluate neurologic outcomes from surgery.

Go to [Neurology.org](#)  for full disclosures.

## Guideline Endorser(s)

American Osteopathic Association - Professional Association

European Federation of Neurological Sciences - Professional Association

## Guideline Status

This is the current release of the guideline.

The American Academy of Neurology (AAN) reaffirmed the currency of the guideline in January 2016.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the [AAN Web site](#) .

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN 55415.

## Availability of Companion Documents

The following are available:

- Periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. Data supplement (e-appendices, e-tables). St. Paul (MN): American Academy of Neurology (AAN); 2013. Available from the [Neurology Web site](#) .
- Periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. AAN summary of evidence-based guidelines for clinicians. St. Paul (MN): American Academy of Neurology; 2013. 2 p. Available in Portable Document Format (PDF) from the [AAN Web site](#) .
- Periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. Case presentation. St. Paul (MN): American Academy of Neurology. 2013. 5 p. Available in PDF from the [AAN Web site](#) .
- Evidence-based guideline: periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. Slide presentation. St. Paul (MN): American Academy of Neurology. 2013. Available from the [AAN Web site](#) .
- Periprocedural management of antithrombotic medications in patients with ischemic cerebrovascular disease. Podcast. St. Paul (MN): American Academy of Neurology (AAN); 2013. Available from the [Neurology Web site](#) .
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the [AAN Web site](#) .

## Patient Resources

The following is available:

- Stroke prevention: managing anticoagulating drugs before having a medical procedure. AAN guideline summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology (AAN). 2013. 3 p. Available in Portable Document Format (PDF) from the [American Academy of Neurology \(AAN\) Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC Status

This NGC summary was completed by ECRI Institute on July 24, 2013. This summary was updated by ECRI Institute on March 10, 2014

following the U.S. Food and Drug Administration advisory on Low Molecular Weight Heparins. The currency of the guideline was reaffirmed by the developer in January 2016 and the summary was updated by ECRI Institute on January 18, 2017.

## Copyright Statement

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## Disclaimer

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